GLOBAL TASK FORCE ON
CHOLERA CONTROL

CHOLERA ROADMAP

RESEARCH AGENDA

JANUARY 2021

TABLE OF CONTENTS

Abbreviations and Acronyms 3
Acknowledgements 4

EXECUTIVE SUMMARY 6
Background 6
Call to Action 6
Results 7

INTRODUCTION 10
Background 10
Goals and Objectives of the Cholera Roadmap Research Agenda 11
Overview of the methodology 11
Results: The research priorities 13

DISCUSSION 19
Elements for success 19
Monitoring the Cholera Roadmap Research Agenda 19
Limitations 20

CALL TO ACTION 21

ANNEX 22
Annex A: Glossary of terms 22
Annex B: Methodology to prioritize research questions for the Cholera Roadmap Research Agenda 23
Annex C: Prioritization analysis of the 93 research questions 25
Annex D: Provisional list of monitoring indicators for the Cholera Roadmap Research Agenda 30
Annex E: Top ten research priorities for respondents from cholera-endemic regions and countries 31

BIBLIOGRAPHY 32

Cover photo: Laboratory technician in Kasese, Uganda, courtesy of Professor David Sack, Johns Hopkins University

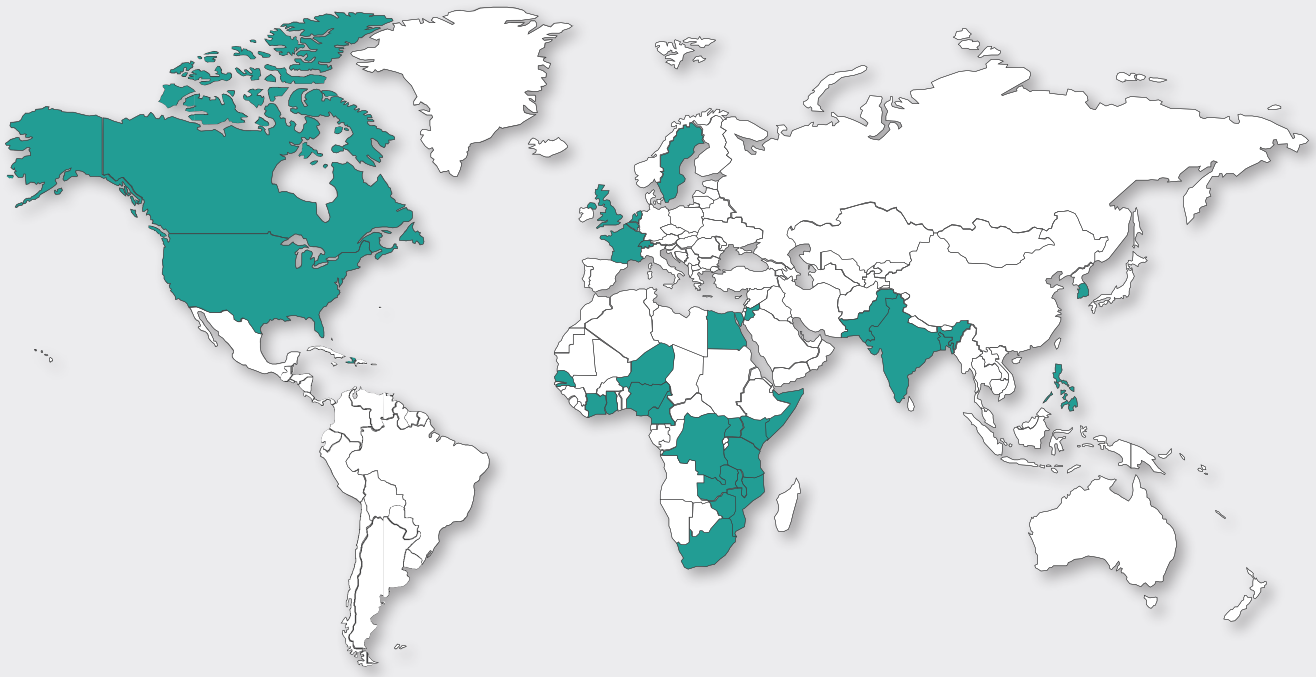
© WHO/Acland

Abbreviations and Acronyms

AEA	average expert agreement
CATI	case-area targeted intervention
CORT	community outbreak response team
CHNRI	Child Health and Nutrition Research Initiative
GTFCC	Global Task Force on Cholera Control
IPC	infection prevention and control
IV	intravenous
NCP	National Cholera Plan
OCV	oral cholera vaccine
ORS/ORT	oral rehydration solution/therapy
PCR	polymerase chain reaction
RDT	rapid diagnostic test
Roadmap	Ending Cholera: A global roadmap to 2030
UNICEF	United Nations Children's Fund
WASH	Water, sanitation and hygiene
WHO	World Health Organization

ACKNOWLEDGEMENTS

This Research Agenda was developed by and for the global cholera control community, with strategic oversight provided by the Cholera Research Agenda Steering Committee: Dominique Legros (Steering Committee Chair, Independent), Abul Kalam Azad (Independent), Philippe Barboza (GTFCC Secretariat, WHO), Val Curtis, (London School of Hygiene & Tropical Medicine), Jan Holmgren (University of Gothenburg), Margot Nauleau (GTFCC Secretariat, WHO), Jose Paulo Langa (National Health Institute, Mozambique) and Daniele Lantagne (Tufts University). As a member of the Global Task Force on Cholera Control (GTFCC), the Wellcome Trust commissioned and supported the development of this document.



The project team and the Cholera Roadmap Research Agenda Steering Committee would like to acknowledge and thank the GTFCC working group chairs, additional experts and the observers of the Cholera Research Agenda Steering Committee for their time and feedback throughout this process, particularly in identifying, developing and refining the research questions. Throughout the entire process, 177 experts provided their time and input to shape the Research Agenda. These experts come from countries in all regions and represent the following organizations:

Action Contre la Faim

African Development Bank

African Medical and Research Foundation

Aga Khan University

Agence Française de Développement (AFD)

Bangladesh Ministry of Health

Bill & Melinda Gates Foundation

Centers for Disease Control and Prevention (US CDC)

Centre de Recherche Médicale et Sanitaire

CERMES, Niger

Centre for Infectious Disease Research in Zambia (CIDRZ)

Christian Medical College, Vellore, India

College of Medicine, University of the Philippines

CommonThread

Community Empowerment Lab

Corps Suisse d'Aide Humanitaire

Ministry of Health, Democratic Republic of the Congo

Foreign, Commonwealth & Development Office (FCDO), UK Government

Directorate General of Health Service, European Civil Protection and Humanitarian Aid Operations (ECHO)

Federal Ministry of Humanitarian Affairs Disaster Management and Social Development, Nigeria

Fondation Veolia Environnement

Fred Hutchinson Cancer Research Center

Gavi, the Vaccine Alliance

GHESKIO Centers

Global Water 2020

Harvard University

icddr,b

ICMR-National Institute of Cholera and Enteric Disease

Imperial College

The INCLEN Trust International

India Council of Medical Research

Institut Pasteur, France

Institut Pasteur, Senegal

Institute of Tropical Medicine

International Federation of Red Cross and Red Crescent Societies (IFRC)

International Medical Corps

International Rescue Committee

International Vaccine Institute (IVI)

Johns Hopkins University

Kenya Medical Research Institute (KEMRI)

King George Medical University

London School of Hygiene & Tropical Medicine

Malawi Ministry of Health
Mass General Hospital Center for Global Health

Medair

Médecins Sans Frontières (MSF)

Fondation Merieux

Ministry of Health, Lusaka

National Department of Health, South Africa

National Health Institute, Mozambique

National Institutes of Health, USA

National Primary Health Care Development Agency, Nigeria

National Institute of Cholera and Enteric Diseases, India

Nigeria Centre for Disease Control

Office of Foreign Disaster Assistance, USA

PATH

Global Polio Eradication Initiative

Postgraduate Institute of Medical Education and Research, India

Première Urgence Internationale

University of Ibadan

Red Cross (Ghana and the Netherlands)

Res'eaux

Rural Water Supply and Sanitation Agency

Save the Children (Bangladesh and USA)

Swedish International Development Cooperation Agency (SIDA)

Society for Applied Studies

Solidarités International

Somalia Ministry of Health

Stockholm International Water Institute

Task Force for Public Health

Tufts University

Uganda Ministry of Health

United Nations Children's Fund (UNICEF)

Université de Dschang

University of Benin

University of Florida

University of Ghana

University of Gothenburg

University of Maryland

University of the Philippines

University of Utah

United States Agency for International Development (USAID)

WaterAid

Wellcome Trust

Wellcome Sanger Institute

World Health Organization (WHO)

Yemen Relief and Reconstruction Foundation

Zambian Permanent Mission

Zimbabwe Ministry of Health

EXECUTIVE SUMMARY

Background

The Global Task Force on Cholera Control (GTFCC) is a partnership of more than 50 institutions, including NGOs, academic institutions and UN agencies, all working together to end cholera.

In October 2017, the partners of the Global Task Force on Cholera Control (GTFCC) endorsed a call to action to end cholera through the implementation of a new strategy known as *"Ending Cholera: A Global Roadmap to 2030"* (the Cholera Roadmap). The Cholera Roadmap champions a multisector approach focused on cholera hotspots that includes the pillars of epidemiology and laboratory (surveillance), oral cholera vaccine (OCV), water, sanitation and hygiene (WASH), case management, and community engagement. The Cholera Roadmap targets a 90% reduction in cholera deaths and cholera elimination in 20 countries by 2030.

In order to achieve the ambitious goals of the Cholera Roadmap, the partners of the GTFCC and cholera-affected countries need to accelerate progress in the coming years. The cholera research community – among the GTFCC partnership's greatest strengths – is eager to contribute generating evidence on the effectiveness of existing tools and interventions and how to optimize their implementation, plus further research into cholera epidemiology and the development of new tools. In response to requests by the cholera control community, GTFCC partners launched a process to develop a prioritized Cholera Roadmap Research Agenda utilizing the Child Health and Nutrition Research Initiative (CHNRI) approach.

The Cholera Roadmap Research Agenda serves as a guide for researchers and donors by providing a prioritized list of research questions that, when answered, will have a significant impact on achieving the Cholera Roadmap goals. The Research Agenda also aims to ensure sufficient and appropriate linkages between research and implementation, making certain that the research and its outputs address the needs of people affected by cholera.

Call to Action

The Cholera Roadmap Research Agenda identified knowledge gaps most important to cholera experts and stakeholders and established a prioritized list of key research questions. This prioritized list was identified through consultations with more than 177 cholera experts and other stakeholders operating at global, regional and country levels, and representing a variety of roles, including researchers, donors, programme implementers and policy-makers.

The GTFCC partners call on all stakeholders to use this Research Agenda as appropriate to their role. For researchers, the document can be used as a tool to prioritize the design and execution of research activities. Donors can use the document as a guide to identify research projects that will have the most impact on practice and policy. Programme implementers can collaborate with researchers to address the priorities and use the research results to address implementation barriers and update their operational plans. National policy-makers can incorporate research priorities and goals into their National Cholera Plans (NCPs) and use research results to strengthen cholera policies and strategies.

Together, the cholera control community can align our efforts and resources to answer the most pressing cholera research questions of our time and encourage discovery research and innovation. This work will provide more effective tools and strategies and a stronger evidence base to accelerate progress towards the goals of the Cholera Roadmap and, ultimately, towards a world free from the threat of cholera.

Results

The Cholera Roadmap Research Agenda identified: 1) The top 20 key priorities across the Roadmap pillars; 2) The top 5 priorities for each pillar; and 3) Key discovery research priority areas.

PILLARS	ORAL CHOLERA VACCINE	WATER, SANITATION & HYGIENE	SURVEILLANCE	COMMUNITY ENGAGEMENT	CASE MANAGEMENT	ALL PILLARS

RANK OVERALL	PILLAR	RESEARCH QUESTION
1		What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?
2		What are potential delivery strategies to optimise oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?
3		Is there additional benefit to adding WASH packages, for example household WASH kits, to an oral cholera vaccine campaign?
4		What is the optimal number of doses of oral cholera vaccine to be used for follow up campaigns in communities previously vaccinated with a 2-dose schedule?
5		Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?
6		What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?
7		What levels of coverage for relevant water, sanitation and hygiene interventions is required in cholera hotspots to control and ultimately eliminate the risk of cholera?
8		What impact does the timing of oral cholera vaccine use have on outbreak prevention and control?
9		What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared to testing only in health facilities?
10		How can the use of oral cholera vaccine in the controlled temperature chain (i.e., outside the cold chain) be leveraged to maximize the coverage or impact of vaccination in a field setting?
11		What is the incremental benefit of implementing a comprehensive interventions package (including water, sanitation and hygiene, antibiotics, oral cholera vaccine, oral rehydration therapy) to reduce cholera mortality during an epidemic?
12		What is the effectiveness and impact of different vaccination strategies for rapid response to cholera outbreaks (e.g., ring vaccination, case-area targeted interventions, etc.)?
13		What is the most cost-effective package of water, sanitation and hygiene, and oral cholera vaccine in different situations, based on transmission dynamics in cholera hotspots?
14		What are the most essential (or what is the minimum set of) infection, prevention and control (IPC) interventions in cholera treatment facilities and oral rehydration points to reduce risk of transmission within these facilities?
15		Are there immunisation strategies other than repeated mass campaigns that will be effective in preventing endemic or epidemic cholera?
16		What is the role and added value of CORTs (community outbreak response teams) in enhancing case investigation and outbreak detection?
17		Can oral cholera vaccine be co-administered safely and without interference with other vaccines during mass campaigns or during routine immunization visits (measles containing vaccines, yellow fever, typhoid, meningitis, pneumococcal conjugate vaccine)?
18		What are effective strategies to scale up the use of household water treatment in controlling cholera outbreaks?
19		How can we improve and fine-tune hotspot definition and identification at a district and sub-district level, such as micro-hotspots?
20		Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?

■ Cross-cutting Research Priorities which involve more than one pillar

Table 2: Overview of the top five research priorities for Case Management

Rank Within Pillar	Research Question
1	What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?
2	What effect does treatment with antibiotics have on cholera transmission?
3	What is the optimal treatment schedule for antibiotic prophylaxis given to household contacts of cholera patients and does this have an effect on the magnitude, transmission and secondary attack rate of cholera outbreaks?
4	What are the common cholera treatment complications in vulnerable populations (for example: pregnant women, the elderly, those with severe acute malnutrition)?
5	Would rehydration solution for malnutrition (ReSoMal[f]) formulated with higher sodium, or standard oral rehydration solution containing high potassium, result in lower mortality or morbidity, compared to the standard WHO rehydration solution, in children with severe acute malnutrition?

Table 3: Overview of the top five research priorities for Epidemiology, Surveillance and Laboratory

Rank Within Pillar	Research Question
1	What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared with testing only in health facilities?
2	How can we improve and fine-tune hotspot definition and identification at a district and sub-district level?
3	What are the optimal designs for surveillance systems (e.g., indicator-based, event-based, community-based, environmental, sentinel site surveillance) to monitor progress of the Cholera Roadmap?
4	What are the optimal surveillance tools (e.g., laboratory methods, case definitions, etc.) to monitor progress of the Cholera Roadmap?
5	How can combined epidemiological and genomic analysis of *V. cholerae* be used to better understand transmission dynamics and inform epidemiological models?

Table 4: Overview of the top five research priorities for OCV

Rank Within Pillar	Research Question
1	What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?
2	What are potential delivery strategies to optimize oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?
3	What is the optimal number of doses of oral cholera vaccine to be used for follow-up campaigns in communities previously vaccinated with a two-dose schedule?
4	Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?
5	What impact does the timing of oral cholera vaccine use have on prevention and control of an outbreak?

Table 5: Overview of the top five research priorities for WASH

Rank Within Pillar	Research Question
1	What levels of coverage for relevant water, sanitation and hygiene interventions is required in cholera hotspots to control and ultimately eliminate the risk of cholera?
2	What are the most essential (or what is the minimum set of) infection prevention and control (IPC) interventions in cholera treatment facilities and oral rehydration points to reduce risk of transmission within these facilities?
3	Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?
4	How can "design thinking" be used to improve the delivery and uptake of water, sanitation and hygiene interventions? Design thinking focuses on understanding the needs of people who will use the intervention and working with them to improve it.
5	What are the factors and determinants that lead to sustainable investments in water, sanitation and hygiene at the country level?

KEY DISCOVERY RESEARCH PRIORITIES

Discovery research can take many years to come to fruition, making it challenging to compare it directly with implementation research that can have a more immediate impact in the field. However, discovery research is no less important and will ultimately be critical to our ability to eliminate cholera.

The three highest priority areas for discovery research are as follows:

Research for the discovery and development of novel and innovative diagnostic tests to increase speed, efficiency and quality of detecting and confirming cholera

Research for the discovery and development of new or improved vaccines to strengthen the bridge between emergency response and long-term cholera control and prevention

Research to contribute to the collection of genomic data to create a global *V. cholerae* sequences database to map and understand long-range transmission routes.

INTRODUCTION

Background

OVERVIEW OF GLOBAL CHOLERA EPIDEMIOLOGY AND BURDEN

Cholera is a diarrhoeal disease that is easily treatable with basic rehydration therapy; however, without treatment, cholera can kill within hours. Although cholera has been eliminated from high-income countries for more than 150 years, it remains an important public health problem and is endemic in many low- and middle-income countries in sub-Saharan Africa, the Middle East and South Asia.

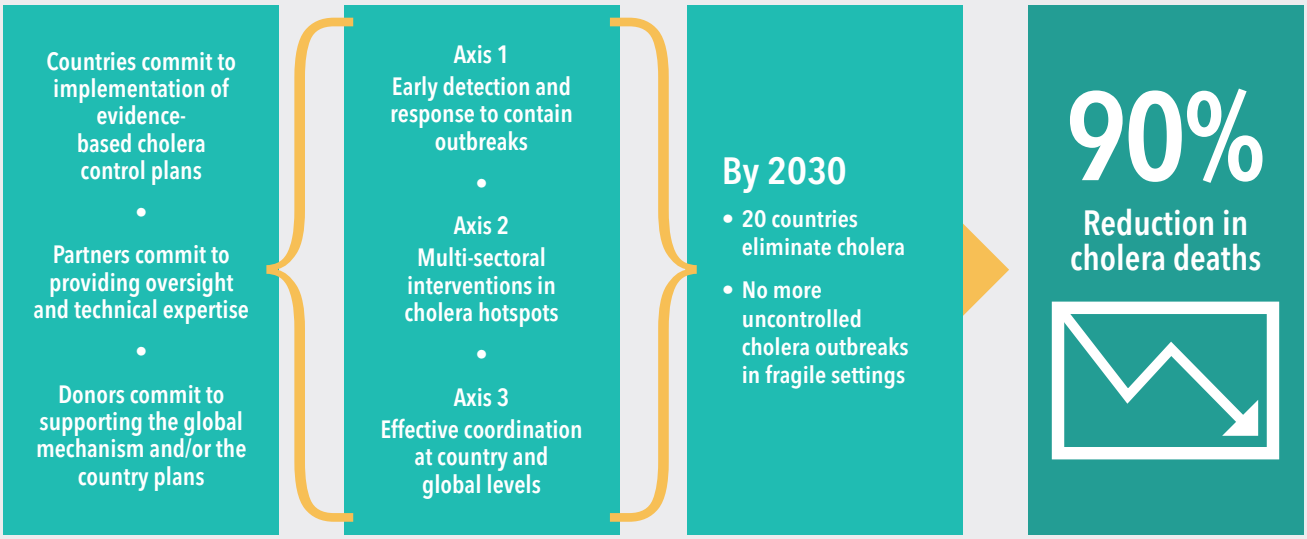
Cholera currently affects an estimated 47 countries across the globe, with large, devastating outbreaks still occurring at regular intervals such as in Zimbabwe in 2008, Haiti in 2010, Sierra Leone in 2012 and the current ongoing outbreak in Yemen.[1,2] Cholera does not happen by chance – it impacts communities already burdened by conflict, lack of infrastructure, poor health systems and malnutrition. Humanitarian emergencies increase the risk of cholera outbreaks. Cholera remains a stark marker of inequity and continues to disproportionately affect the poorest and most vulnerable populations around the world and within each affected country.[3]

Cholera is caused by the *Vibrio cholerae (V. cholerae)* bacterium and is usually transmitted through faecally contaminated water or food. Of the more than 200 serogroups, only serogroups O1 and O139 have been linked to outbreaks. The consequences of infection can range from asymptomatic carriage to severe acute watery diarrhoea, depending on several factors including the amount of *V. cholerae* bacteria ingested, prior exposure or vaccination, pregnancy, immunocompromised state, etc.[4] *V. cholerae* can be detected by rapid diagnostic tests (RDTs). However, isolation and identification of *V. cholerae* from faecal samples by culture or polymerase chain reaction (PCR) remains the standard test for cholera diagnosis and case confirmation.[5]

LAUNCH OF ENDING CHOLERA: A GLOBAL ROADMAP TO 2030

In October 2017, the Global Task Force on Cholera Control (GTFCC) endorsed a global strategy to end cholera through the implementation of "Ending Cholera: A Global Roadmap to 2030" (the Cholera Roadmap). The Cholera Roadmap operationalizes a global strategy for control at the country level and provides a concrete path towards a world where cholera is no longer a public health threat.

THEORY OF CHANGE OF THE GLOBAL ROADMAP



The Cholera Roadmap utilizes a multisector approach of the following pillars: epidemiology and laboratory (surveillance) to detect and monitor the disease, oral cholera vaccine (OCV) and water, sanitation and hygiene (WASH) to prevent the disease and respond to outbreaks, case management to treat the disease and community engagement to improve the uptake of al interventions. The main goal of the Roadmap is to reduce cholera deaths by 90% and eliminate the disease in 20 countries by 2030.[3]

When the Cholera Roadmap was launched in 2017, there were an estimated 2.9 million cases of cholera and 95,000 deaths per year worldwide.[1] Since that time, cholera-affected countries have made significant progress in the fight against cholera with the support of GTFCC partners. Major outbreaks in Haiti and the Horn of Africa have been brought under control. Humanitarian crises that may once have resulted in large cholera outbreaks, such as the 2019 cyclone in Mozambique and the Rohingya refugee crisis, did not lead to outbreaks thanks to rapid action by governments and partners.[6]

With the launch of the Cholera Roadmap, it became clear that additional evidence on the effectiveness of existing tools and interventions and how to optimize their implementation, plus further research into cholera epidemiology and the development of new tools, would greatly aid countries' ability to implement the Cholera Roadmap and achieve their control and elimination goals. Research outputs can provide relevant data and evidence to inform policies and practices, and ultimately shape how countries prevent and respond to cholera and therefore protect their populations from the disease. The first step to achieving this is to identify and prioritize the most impactful research activities that will aid those working in cholera to support the implementation of the Cholera Roadmap.

The Cholera Roadmap Research Agenda aims to accelerate progress towards the Cholera Roadmap goals by assisting:

- **international and national research donor agencies** to identify research projects that will have the most impact on practices and policy;
- **researchers** to prioritize the design and execution of research activities that will lead to evidence and implementable interventions with the most impact;
- **programme implementers** working on implementing the Cholera Roadmap to collaborate with researchers and to use the research results to address implementation barriers and update their operational plans;
- **policy-makers** to incorporate relevant research goals into their NCPs and to use the research results to strengthen cholera policies and strategies.

Goals and objectives of the Cholera Roadmap Research Agenda

The Cholera Roadmap Research Agenda seeks to fill important evidence gaps by identifying and prioritizing research questions, attracting donor funds, and encouraging sufficient and appropriate linkages between research and implementation so that research and evidence address the needs of people implementing the Cholera Roadmap and the populations most affected by cholera.

Overview of the methodology

A consultative approach based on the Child Health and Nutrition Research Initiative (CHNRI) methodology was selected to identify cholera research priorities in a transparent, consultative, comprehensive and replicable way.[7–16] CHNRI has been developed and refined over many years and has been used to prioritize a variety of health research topics. The first phase of work focused on tailoring the CHNRI methodology to the Cholera Roadmap, while the second phase focused on prioritizing the research questions. Additional details on the methodology may be found in Annex B.

PHASE 1: TAILORING THE METHODOLOGY TO THE CHOLERA ROADMAP

Consultation of key cholera stakeholders[a] was conducted through interviews or surveys and aimed to obtain feedback on selecting the prioritization criteria, refining their descriptions and collecting research questions. The feedback was collated and analysed from a qualitative and quantitative perspective.

In parallel, research questions were identified based on existing work and additional feedback from the GTFCC working groups, public sources of data,[4,17] and consultations. The potential research questions were reviewed through an iterative process with the GTFCC working group chairs and key experts.[b] This process aimed to remove duplications, refine the language and identify questions where sufficient evidence was already available. Each of the final research questions was reviewed and assigned to the relevant Roadmap pillar(s): (i) case management; (ii) community engagement; (iii) epidemiology and laboratory (surveillance); (iv) OCV; and (v) WASH. In some situations, research questions were relevant to more than one Roadmap pillar and these questions were classified as "cross-cutting". All research questions with a community engagement component were linked to one, or all pillars, demonstrating the importance of integrating community engagement activities as part of each pillar. Therefore, community engagement research questions were also defined as "cross-cutting", as they underpin the success of cholera control and elimination strategies.

Virtual meetings were held with key stakeholders (representatives from research, implementing partners, policy-makers and donors) to finalize the context and criteria. To determine weights for the criteria, an online survey was sent to experts asking them to distribute 100 points across five criteria based on perceived level of importance. The proposed weights were determined by dividing the mean values allocated to each criterion by 20.

PHASE 2: PRIORITIZING THE RESEARCH QUESTIONS

An online survey was designed for cholera experts to evaluate and score each of the research questions. The respondents were given four potential options of "Yes", "No", "Maybe" and "Don't know" for each of the prioritization criteria. Each response was assigned points with "Yes", "No" and "Maybe" receiving 1.0, 0 and 0.5 points, respectively. The "Don't know" responses were excluded from the calculation of the weighted research priority score and reviewed separately. The weighted research priority score was calculated on a scale of 0% to 100% with rankings assigned to each question based on the score. In addition, stratified analyses[c] were conducted to evaluate potential differences in scoring by stakeholder groups.

The priorities for the Research Agenda were chosen based on the weighted research priority score and considered all responses from all of the cholera experts. The key priorities were based on the top 20 highest scoring research questions across all pillars. Separate lists for each Roadmap pillar were based on the five highest-scoring research questions per pillar to ensure alignment with the GTFCC working groups and their mandates.

OCV distribution in Chikwawa, Malawi © Lorenzo Pezzoli

[a] Individuals include those engaged with the GTFCC network, from cholera research grants and publications, and experts from other diseases with elimination goals.

[b] Experts included members of the GTFCC Independent Review Panel.

[c] Stratified analyses were conducted considering the location of the respondent to identify the "immediate needs" of those working in cholera-endemic countries.

Results: The research priorities

DEFINING THE CRITERIA AND CONTEXT FOR RESEARCH PRIORITIZATION

As part of Phase 1, 141 individuals from 32 countries were consulted, resulting in the identification of 93 research questions representing all the Roadmap pillars (see Annex C for complete list).

Consultations with stakeholders also defined both the Research Agenda context and the five different criteria for prioritizing research (see text box at right). The context defined the scope of the Research Agenda to enable consistency in scoring across multiple stakeholders. Five criteria were selected as valuable and necessary measures to prioritize research for cholera and were weighted to demonstrate their relative importance to one another.

PRIORITIZING THE RESEARCH QUESTIONS

To prioritize research for cholera, 138 cholera experts in 33 countries scored the research questions using the context and criteria (full results in Annex C). These experts were based predominantly in the WHO regions of Africa, the Americas, Europe and South-East Asia, with the majority of responses from implementing partners[d] (including governments) and researchers working in the areas of epidemiology and laboratory/surveillance, OCV and WASH. See Figure 1 for full demographics.

Key priorities for the Cholera Roadmap Research Agenda

Based on the prioritization scoring results, the 20 highest-scoring research questions (Table 1) were identified as the key research priorities across all Roadmap pillars used the collective knowledge and opinion of 138 cholera experts, including 68 stakeholders located in cholera-endemic countries or regions. The key priorities highlight that research should be focused on:

- Optimizing the delivery of existing interventions to maximize impact on populations in need
- Developing new interventions/strategies improving the effectiveness of existing interventions/strategies.

The table on page 14 provides the 20 key priorities for the Cholera Roadmap Research Agenda.

Cholera Roadmap Research Agenda contextual factors and prioritization criteria

Contextual factors:

- **Population of interest:** All countries and communities where cholera is endemic and/or there is epidemic risk of cholera.
- **Time scale:** Present day to 2030.
- **Geographic scope of research:** Global, regional, national and subnational levels. Subnational may include different administrative levels, such as provinces or states, districts, communities or households.
- **Impact of interest:** Reduction of deaths and burden of cholera. Burden may include morbidity as well as any economic or social impact of cholera.

Criteria to score the research questions:

- **Answerability (weight: 0.79):** Do you think the proposed research is answerable in cholera-affected countries and communities?
- **Impact (1.20):** Will the research outputs contribute to reducing cholera deaths and burden?
- **Implementability (1.12):** Will the proposed research lead to solutions that are implementable (e.g., feasibility of introduction, including acceptability to the cholera-affected communities and scale up)?
- **Relevancy (1.06):** Will the proposed research contribute to addressing relevant evidence gaps in the cholera-affected countries or communities when implementing the Cholera Roadmap?
- **Sustainability (0.83):** Will the proposed research lead to solutions that are sustainable over time without, or with only limited, external financial or technical support in cholera-affected countries?

[d] Implementing partners includes United Nations organizations, bilateral development organizations, international organizations, non-governmental organizations, civil society organizations and governmental departments of non-cholera-endemic countries (e.g., the Centers for Disease Control and Prevention of the United States).

Table 1: Key priorities for the Cholera Roadmap Research Agenda

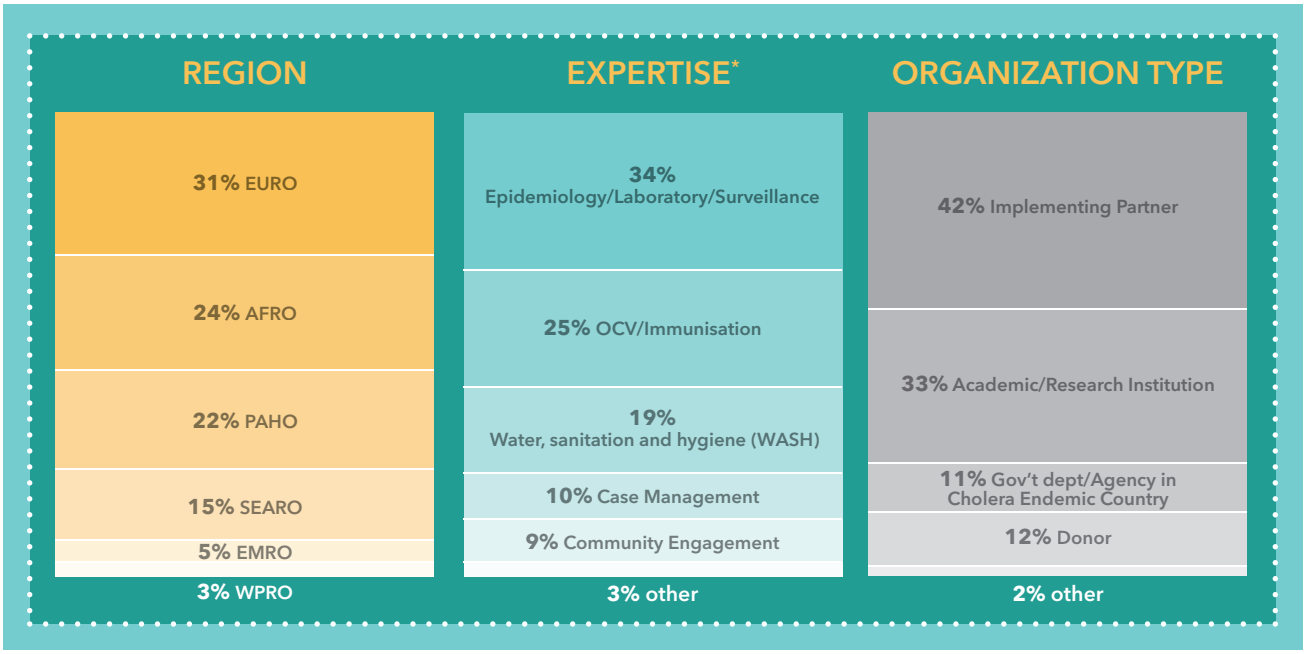
PILLARS	ORAL CHOLERA VACCINE	WATER, SANITATION & HYGIENE	SURVEILLANCE	COMMUNITY ENGAGEMENT	CASE MANAGEMENT	ALL PILLARS

RANK OVERALL	PILLAR[e]	RESEARCH QUESTION		WEIGHTED RESEARCH PRIORITY SCORE
1		What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?	⚑	88.8%
2		What are potential delivery strategies to optimise oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?	⚑	87.4%
3		Is there additional benefit to adding WASH packages, for example household WASH kits, to an oral cholera vaccine campaign?	⚑	87.1%
4		What is the optimal number of doses of oral cholera vaccine to be used for follow up campaigns in communities previously vaccinated with a 2-dose schedule?		86.9%
5		Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?	⚑	86.8%
6		What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?	⚑	86.8%
7		What levels of coverage for relevant water, sanitation and hygiene interventions is required in cholera hotspots to control and ultimately eliminate the risk of cholera?	⚑	86.3%
8		What impact does the timing of oral cholera vaccine use have on outbreak prevention and control?		86.2%
9		What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared to testing only in health facilities?	⚑	86.1%
10		How can the use of oral cholera vaccine in the controlled temperature chain (i.e., outside the cold chain) be leveraged to maximize the coverage or impact of vaccination in a field setting?	⚑	85.9%
11		What is the incremental benefit of implementing a comprehensive interventions package (including water, sanitation and hygiene, antibiotics, oral cholera vaccine, oral rehydration therapy) to reduce cholera mortality during an epidemic?	⚑	85.7%
12		What is the effectiveness and impact of different vaccination strategies for rapid response to cholera outbreaks (e.g., ring vaccination, case-area targeted interventions, etc)?	⚑	85.3%
13		What is the most cost-effective package of water, sanitation and hygiene, and oral cholera vaccine in different situations, based on transmission dynamics in cholera hotspots?	⚑	85.2%
14		What are the most essential (or what is the minimum set of) infection, prevention and control (IPC) interventions in cholera treatment facilities and oral rehydration points to reduce risk of transmission within these facilities?		84.9%
15		Are there immunisation strategies other than repeated mass campaigns that will be effective in preventing endemic or epidemic cholera?	⚑	84.9%
16		What is the role and added value of CORTs (community outbreak response teams) in enhancing case investigation and outbreak detection?	⚑	84.6%
17		Can oral cholera vaccine be co-administered safely and without interference with other vaccines during mass campaigns or during routine immunization visits (measles containing vaccines, yellow fever, typhoid, meningitis, pneumococcal conjugate vaccine)?		84.3%
18		What are effective strategies to scale up the use of household water treatment in controlling cholera outbreaks?	⚑	84.1%
19		How can we improve and fine-tune hotspot definition and identification at a district and sub-district level, such as micro-hotspots?		84.1%
20		Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?	⚑	84.0%

■ Cross-cutting Research Priorities which involve more than one pillar

⚑ Ranked within the top 20 research priorities for those based on cholera-endemic locations

Figure 1: Respondent Demographics



* Given that cholera experts often have overlapping expertise and experiences (e.g., epidemiology is often a complementary expertise to other Roadmap pillar areas), the survey respondents were allowed to choose up to two areas of expertise.

Given extensive consultations with those located in cholera-endemic countries or regions (N = 68), a stratified analysis considering only their responses was conducted to identify their top 20 research priorities. The majority of these (15/20) align with the top 20 key research priorities and are indicated in Table 1 with a symbol, demonstrating a strong country-level need for this research evidence. The ranked list of research priorities considering only the perspectives of country-level respondents is also available as a separate list in Annex E. Researchers and donors may wish to consider this order of priorities, plus two additional research questions on the knowledge, attitudes and practices in the community relating to OCV and the optimal environmental surveillance for *V. cholerae*, when identifying evidence gaps to inform their research objectives and goals.

The multi-sectoral strategy delineated in the Cholera Roadmap means that cross-cutting research will play an especially crucial role in achieving our shared goals. Five of the top 20 key research priorities identified in the Cholera Roadmap Research Agenda take a cross-pillar approach (as highlighted in Table 1), recognizing the importance of using research to foster and strengthen the multisectoral approach of the Cholera Roadmap. These cross-cutting research priorities focus on how to:

- improve outbreak detection and investigation
- bridge short-term interventions to longer-term cholera control and elimination
- communicate the benefits of utilizing the multisectoral Cholera Roadmap approach
- use community engagement to sustain WASH interventions.

Although the goals of ending cholera are within our reach using existing tools, discovery research which seeks to generate new knowledge or develop novel interventions could significantly shift implementation of the Cholera Roadmap, as well as accelerate and sustain achievements towards cholera elimination beyond 2030. During phase 1, three priority areas for discovery research were identified as essential for continued action. It is important to ensure that these areas receive early investment, as discovery research generally has longer timelines to translate its results into evidence or interventions (see textbox on page 16).

Discovery research can take many years to come to fruition, making it challenging to compare directly with implementation research that can have a more immediate impact in the field. However, discovery research is no less important and will be ultimately critical to our ability to eliminate cholera. The three highest priorities for discovery research are as follows:

- research for the discovery and development of novel and innovative diagnostic tests to increase speed, efficiency and quality of detecting and confirming cholera;
- research for the discovery and development of new or improved vaccines to strengthen the bridge between emergency response and long-term cholera control and prevention; and
- research to contribute to the collection of genomic data to create a global *V. cholerae* sequence database to map and understand long-range transmission routes.

Top five priorities per Roadmap pillar

In alignment with the Cholera Roadmap and the GTFCC working groups, the top five highest-scoring research questions for four Roadmap pillars – case management; epidemiology and laboratory (surveillance) ; OCV; and WASH – were used to form pillar-specific research priority lists. Some of the questions that ranked within the top five of the Roadmap pillars are also included as part of the top 20 key priorities. All community engagement research questions were considered "cross-cutting", however, the top five priorities for community engagement have not been separated, but can be found in the full list of research questions (Annex C).

Case management

Effective case management is critical to saving lives, as cholera can be treated with ORS/ORT, intravenous fluids and antibiotics, and, therefore, any deaths due to cholera are avoidable tragedies. The identified case management research priorities **focus on improving the ability to address these barriers**, such as utilizing community health workers as part of integrated case management and identifying the best treatment protocols (e.g., if and how the inclusion of antibiotics can improve treatment outcomes). See Table 2 for additional details on case management research priorities.

The Cholera Roadmap seeks to empower countries and communities and engage them in identifying problems and opportunities for preventing and controlling cholera. Thus, community engagement activities remain an important driver to the success of the Cholera Roadmap and should be integrated into as many research questions as possible and not considered a stand-alone activity. Research priorities that utilize community engagement approaches are marked with this symbol:

Table 2: Overview of the top five research priorities for Case Management

Rank Within Pillar	Research Question	Weighted Research Priority Score
1	What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?	86.8%
2	What effect does treatment with antibiotics have on cholera transmission?	83.3%
3	What is the optimal treatment schedule for antibiotic prophylaxis given to household contacts of cholera patients and does this have an effect on the magnitude, transmission and secondary attack rate of cholera outbreaks?	80.5%
4	What are the common cholera treatment complications in vulnerable populations (for example: pregnant women, the elderly, those with severe acute malnutrition)?	80.2%
5	Would rehydration solution for malnutrition (ReSoMal[f]) formulated with higher sodium, or standard oral rehydration solution containing high potassium, result in lower mortality or morbidity, compared to the standard WHO rehydration solution, in children with severe acute malnutrition?	80.1%

[f] ReSoMal is a powder for the preparation of an oral rehydration solution exclusively for oral or nasogastric rehydration of people suffering from severe acute malnutrition. It must be used exclusively under medical supervision in inpatient care and must not be given for free use to the mother or caregiver.

Epidemiology, surveillance and laboratory capacity

Strong disease surveillance and laboratory capacity, coupled with a solid understanding of cholera epidemiology, will help countries to stop cholera in its tracks by quickly detecting cholera and identifying and monitoring hotspots to target Cholera Roadmap interventions. Strong surveillance and laboratory capacity also play a role in monitoring the effectiveness and impact of Cholera Roadmap interventions and NCPs. The prioritized research questions **focus on addressing the challenges in rapidly detecting cholera outbreaks and improving the systems, tools and data to identify and monitor progress in hotspots,** which ultimately focuses resources to the most-at-risk communities. See Table 3 for additional details on epidemiology, surveillance and laboratory research priorities.

Table 3: Overview of the top five research priorities for Epidemiology, Surveillance and Laboratory

Rank Within Pillar	Research Question	Weighted Research Priority Score
1	What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared with testing only in health facilities?	86.1%
2	How can we improve and fine-tune hotspot definition and identification at a district and sub-district level?	84.1%
3	What are the optimal designs for surveillance systems (e.g., indicator-based, event-based, community-based, environmental, sentinel site surveillance) to monitor progress of the Cholera Roadmap?	83.8%
4	What are the optimal surveillance tools (e.g., laboratory methods, case definitions, etc.) to monitor progress of the Cholera Roadmap?	82.8%
5	How can combined epidemiological and genomic analysis of *V. cholerae* be used to better understand transmission dynamics and inform epidemiological models?	81.2%

Oral cholera vaccine

OCV is a safe, inexpensive and effective tool that serves as the bridge to emergency response and longer-term WASH-based cholera prevention and control. Key implementation challenges currently include **how to efficiently and effectively use OCV** in the populations most at risk. The key research priorities identified aim to fill these knowledge gaps related to understanding OCV impact in younger children and identifying the best strategies to optimize OCV delivery, including coverage in hard-to-reach populations.

Table 4: Overview of the top five research priorities for OCV

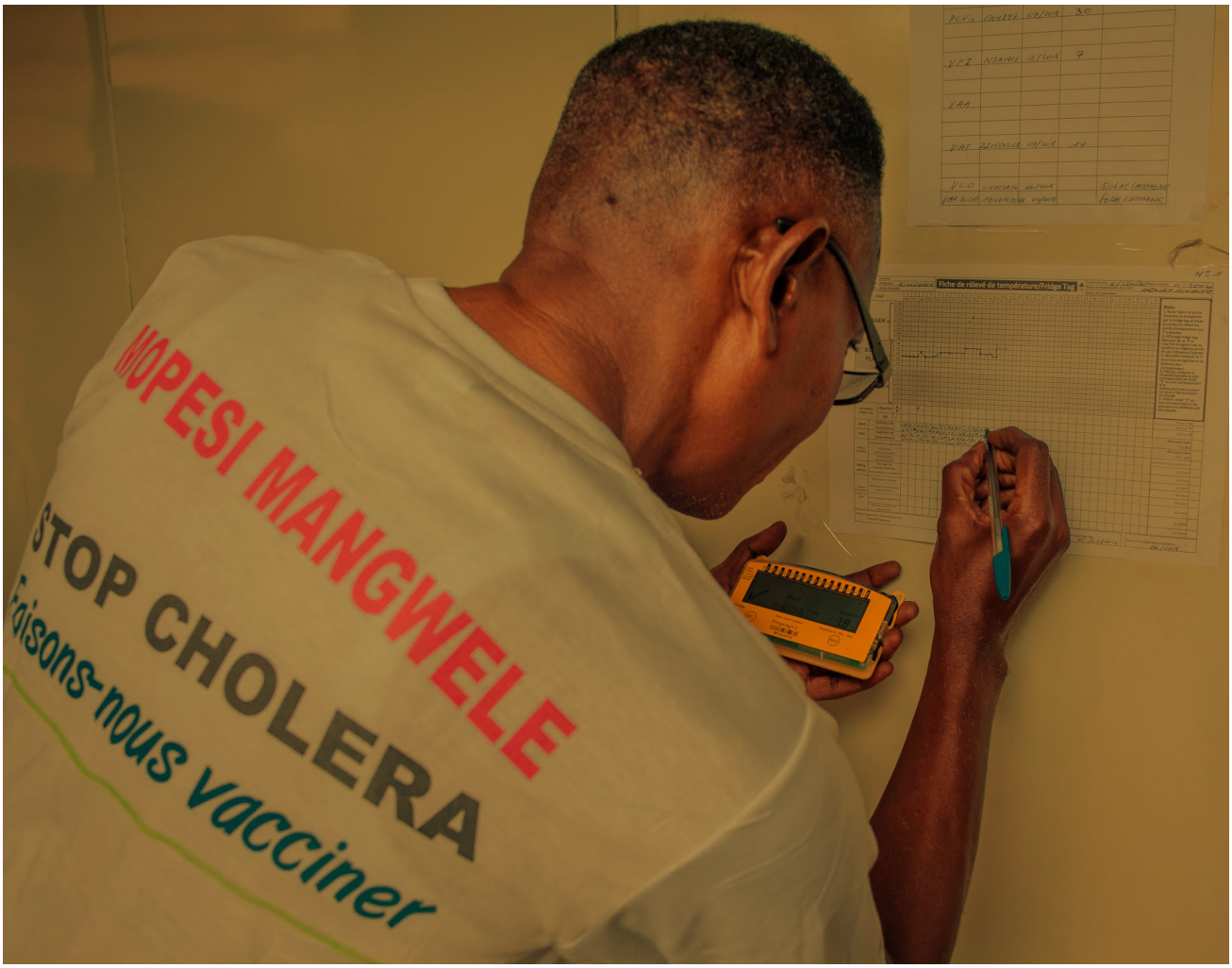
Rank Within Pillar	Research Question	Weighted Research Priority Score
1	What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?	88.8%
2	What are potential delivery strategies to optimize oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?	87.4%
3	What is the optimal number of doses of oral cholera vaccine to be used for follow-up campaigns in communities previously vaccinated with a two-dose schedule?	86.9%
4	Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?	86.8%
5	What impact does the timing of oral cholera vaccine use have on prevention and control of an outbreak?	86.2%

Water, sanitation and hygiene

WASH services are currently the only long-term solution to end cholera and many other water-borne diseases. The prioritized research questions focus on addressing key evidence gaps regarding **which type and what level of WASH interventions are needed to eliminate the risk of cholera.**

Table 5: Overview of the top five research priorities for WASH

Rank Within Pillar	Research Question	Weighted Research Priority Score
1	What levels of coverage for relevant water, sanitation and hygiene interventions is required in cholera hotspots to control and ultimately eliminate the risk of cholera?	86.3%
2	What are the most essential (or what is the minimum set of) infection prevention and control (IPC) interventions in cholera treatment facilities and oral rehydration points to reduce risk of transmission within these facilities?	84.9%
3	Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?	84.0%
4	How can "design thinking" be used to improve the delivery and uptake of water, sanitation and hygiene interventions? Design thinking focuses on understanding the needs of people who will use the intervention and working with them to improve it.	83.0%
5	What are the factors and determinants that lead to sustainable investments in water, sanitation and hygiene at the country level?	80.3%



Personnel record the results of a 2016 OCV campaign in Kinshasa, DRC. © Lorenzo Pezzoli

DISCUSSION

The development of the Cholera Roadmap Research Agenda not only helped to identify the knowledge gaps that are most important to cholera experts and stakeholders, but also establishes a prioritized list of key research questions. To support the implementation of the Cholera Roadmap, 93 research questions were first identified and then scored. Overall, 177 people helped to shape the Cholera Roadmap Research Agenda through involvement in one or both phases. The following priorities were identified:

- 20 key priorities spanning all areas of cholera research, including priorities that aim to fill gaps related to the Cholera Roadmap's multisectoral approach and cross-cutting community engagement interventions
- top five priorities for case management, epidemiology and laboratory/surveillance, OCV and WASH
- three essential areas for discovery research.

There are increasing calls for research that looks across multiple Roadmap pillars to answer key questions on implementation, particularly from country-level respondents, as well as among donors and programme implementers.

Elements for success

During the development of the Cholera Roadmap Research Agenda, key elements were consistently identified by stakeholders as necessary to ensure the success of the Cholera Roadmap and the corresponding research agenda.

Partnership and collaboration with country stakeholders

- Engage governments of cholera-affected countries to ensure that the evidence produced from research is used to inform decision-making, policies, strategies and practices, and to advocate for the value and relevance of research.
- Strengthen country capacity to identify, finance and implement locally relevant research activities, including earlier involvement of country stakeholders in research activities.

Sustainability and implementability of research outputs

- Establish a balance between prevention and control research that focuses on proactive measures to prevent cholera outbreaks and reactive measures to improve timely detection and response.
- Consider existing health system structures and capacity when designing research activities to ensure that research outputs can be sustainably implemented in cholera-affected countries and attain the required levels of coverage and uptake to maximize impact.

Ethics and equity

- Maintain ethics and equity as key principles in all research activities. Ensure that all research protocols are subject to ethics reviews by the relevant institutional committees and consider an equity lens when reviewing research protocols, given that cholera is a highly sensitive and specific indicator for inequities.

Monitoring the Cholera Roadmap Research Agenda

The identified research priorities may evolve or change over time. These changes may be driven by questions being answered or by major and unpredictable shifts (e.g., natural disasters, large humanitarian emergencies) that affect the cholera landscape and ultimately the research needs. Continuous monitoring and reporting on the progress and needs of cholera-endemic countries can serve as a guide to when a refresh of the research priorities is needed. In addition, monitoring will measure the impact of the Cholera Roadmap Research Agenda and determine whether the identified gaps have been filled.[16]

Children stand beside a hand-washing station and a chlorine dispenser in a compound in which households were covered under icddr,b's Cholera Vaccine Behavior Modification (CVBM) study in the Mirpur locality, Dhaka, Bangladesh. ©Bill & Melinda Gates Foundation/Prashant Panjiar

Provisional indicators have been developed to monitor the following aspects (see Annex D for additional details):

- Research Agenda **awareness** monitors the level of awareness and support for the Cholera Roadmap Research Agenda and the identified priorities;
- Research Agenda **use and uptake** monitors the extent that the identified priorities are used by researchers, donors and other stakeholders to inform decision-making, demonstrate the relevancy of research, allocate research funding and ensure integration within NCPs; and
- Research Agenda **outputs** monitor the completion and publication of results from research addressing the prioritized questions.

Limitations

Although the application of the CHNRI methodology ensures results that are transparent, consultative, comprehensive and replicable, it has limitations. The identification of the evidence gaps relied heavily on inputs obtained during the GTFCC working group meetings, as well as additional consultations with experts. This approach may not have captured all of the evidence gaps, but instead has the benefit of identifying gaps that reflect the needs of cholera experts and stakeholders.

Overall, 177 cholera experts[9] were involved in shaping the Research Agenda at various stages, however, there was suboptimal representation from certain important stakeholder groups, such as experts from governments in cholera-affected countries and unequal representation across all Roadmap pillars, with particularly high representation from immunization and epidemiology/surveillance experts.

[9] Response rates differed between the two phases of developing the Research Agenda. Overall, 141 experts were consulted in Phase 1 and 138 experts scored the research questions in Phase 2 with some, but not total, overlap.

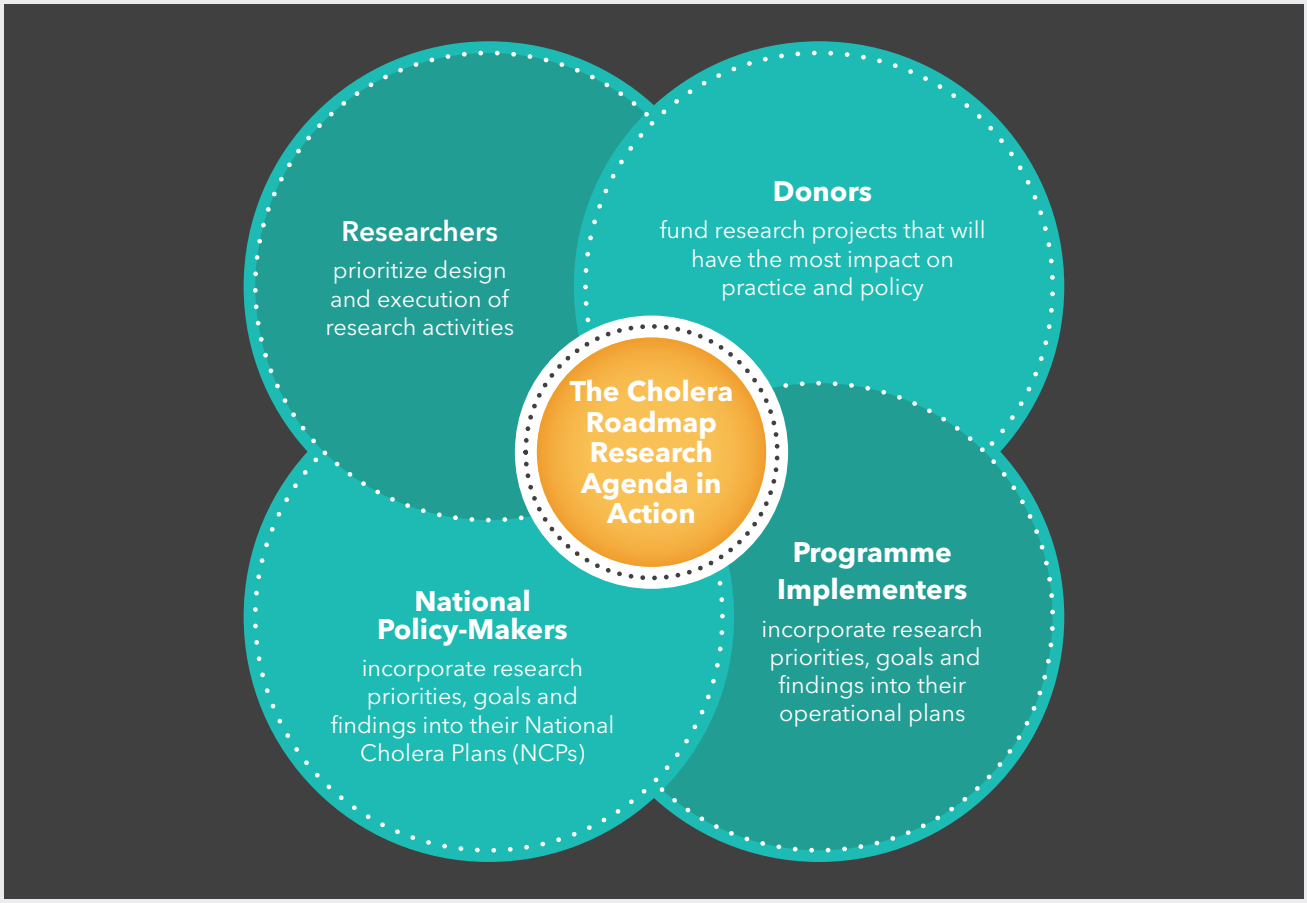
CALL TO ACTION

The Cholera Roadmap Research Agenda identified knowledge gaps most important to cholera experts and stakeholders and established a prioritized list of key research questions. This prioritized list was identified through consultations with more than 177 cholera experts and other stakeholders operating at global, regional and country levels, and representing a variety of roles, including researchers, donors, programme implementers and policy-makers.

The GTFCC partners calls on all stakeholders to use this Research Agenda as appropriate to their role. For researchers, the document can be used as a tool to prioritize the design and execution of research activities. Donors can use the document as a guide to identify research projects that will have the most impact on practice and policy. Programme implementers can collaborate with researchers to address the priorities and use the research results to address implementation barriers and update their operational plans. National policy-makers can incorporate research priorities and goals into their (NCPs) and use research results to strengthen cholera policies and strategies.

Together, the cholera control community can align our efforts and resources to answer the most pressing cholera research questions of our time and encourage discovery research and innovation. This work will provide a stronger evidence base and more effective tools and strategies to accelerate progress towards the goals of the Cholera Roadmap and, ultimately, towards a world free from the threat of cholera.

Figure 2: Call to Action



ANNEX

Annex A: Glossary of terms

Case-area targeted interventions (CATI)[18]

Cholera prevention and control interventions targeted to contacts and neighbours of cholera cases, including improved water, sanitation and hygiene (WASH), oral cholera vaccine (OCV) and prophylactic antibiotics.

Cholera elimination[19]

Any country that reports no confirmed cases with evidence of local transmission for at least three consecutive years and has a well-functioning epidemiologic and laboratory surveillance system able to detect and confirm cases.

Cholera-endemic area[19]

An area where confirmed cholera cases, resulting from local transmission, have been detected in the past three years. An area can be defined as any subnational administrative unit including state, district or smaller localities. Any country that contains one or more subnational administrative units that are endemic, as defined above, is considered a cholera-endemic country.

Cholera hotspot[19]

A geographically limited area (such as a city, administrative level 2 or health district catchment area) where environmental, cultural and/or socioeconomic conditions facilitate the transmission of the disease and where cholera persists or reappears regularly. Hotspots play a central role in the spread of the disease to other areas.

Cholera outbreak[19]

A cholera outbreak is defined by the occurrence of at least one confirmed case of cholera and evidence of local transmission. In areas with sustained transmission (year-round), a cholera outbreak is defined as an unexpected increase (in magnitude or timing) of suspected cases, over two consecutive weeks, of which some are laboratory confirmed.

Cholera serogroup[4]

There are > 200 serogroups of *V. cholerae*, distinguished by the polysaccharides of the somatic (O) antigen. Of these, only two serogroups, toxigenic O1 and O139, cause epidemic disease and there is no proven cross-protection between O1 and O139. Serogroup O1 has two biotypes, El Tor and classical O1. El Tor is responsible for the seventh cholera pandemic that started in 1961 and persists longer in the environment. It is associated with a higher rate of asymptomatic or mild cases and is shed for longer and in higher numbers in the faeces.

Community outbreak response teams (CORT)[20]

A team of disease experts that utilize epidemiological and surveillance data to target cholera-affected households and at-risk populations in communities to design and implement measures to reduce or "slow down" cholera transmission as quickly as possible.

Genotype[21]

The genetic makeup, as distinguished from the phenotype, of an organism or a group of organisms.

Implementation[22]

The act of putting a plan into action or starting to use something. For the Cholera Roadmap Research Agenda, it refers to the act of putting into action Cholera Roadmap interventions and making cholera-related services and products available to populations in need.

Intervention[23]

A health intervention is an act performed for, with or on behalf of a person or population whose purpose is to assess, improve, maintain, promote or modify health functioning or health conditions. For the Cholera Roadmap Research Agenda, this refers to the multisectoral approach based on epidemiology, laboratory and surveillance, OCV, WASH, case management and community engagement.

Phenotype[21]

The observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences.

Prophylaxis[22,24]

Treatment or action taken to prevent a disease. For the Cholera Roadmap Research Agenda, this generally refers to antibiotic prophylaxis or zinc prophylaxis.

ReSoMal[25]

ReSoMal is a powder for the preparation of an oral rehydration solution exclusively for oral or nasogastric rehydration of people suffering from severe acute malnutrition. It must be used exclusively under medical supervision in inpatient care, and must not be given for free use to the mother or caregiver.

Sero-surveillance

Sero-surveillance consists of systematic sampling to obtain serum samples from a representative population group and test it for the prevalence of serological markers (usually circulating antigen or antibody) for specific pathogens to describe the past exposure or immunity to the pathogen.

Annex B: Methodology to prioritize research questions for the Cholera Roadmap Research Agenda

PHASE 1: TAILORING THE CHNRI METHODOLOGY

Stakeholders were identified through the GTFCC network, from cholera research grants and from publications. Key experts from other diseases with elimination goals were also consulted. Consultations aimed to ensure that the Cholera Roadmap Research Agenda reflected the opinions and experiences of individuals working in cholera-affected countries. The consultations identified:

- barriers to the implementation of the Roadmap, which were converted into research questions; and
- prioritization criteria considered the most important for evaluating the research questions.[h]

The consultations were structured using predefined questions where the respondents rated each of the proposed criteria and their description using a Likert scale of "Not Important at All" to "Extremely Important". A mean was calculated for each criterion based on applying points of 1 for "Not Important at All" to 5 for "Extremely Important".

The qualitative feedback from the consultations were combined and a thematic analysis was conducted to identify key themes related to the criteria. These themes were then used to select the five prioritization criteria and adjust their descriptions to better reflect the Cholera Roadmap needs.

Methodology to collect and refine the research questions

Research questions that had been previously identified by the GTFCC working groups were collected, compiled and supplemented with new questions identified during the consultation phase. Bilateral discussions with key experts and the GTFCC working group chairs were held to refine the language, remove any duplicate questions or identify questions where sufficient evidence already existed. Each research question was reviewed and assigned to the relevant Roadmap pillars of (i) case management; (ii) community engagement; (iii) epidemiology and laboratory/surveillance; (iv) oral cholera vaccines; and (v) water, sanitation and hygiene, as well as the 4D framework from CHNRI.[10]

[h]The experts provided feedback on the description of the criteria, whether each should be used to prioritize research questions and rate their level of importance using a Likert scale of 1 to 5 (1 being not important at all and 5 being extremely important, noting that each criterion was rated independent of the others).

Methodology to develop the contextual factors and select the criteria used for prioritization and their relevant weights

Based on the feedback obtained from the consultations, the contextual factors and prioritization criteria were further refined via a stakeholder meeting.

The contextual factors determine the scope of the research within the Cholera Roadmap Research Agenda, focusing on the who, when, where and what outcomes are needed from the research activities. As the research questions will be interpreted based on individual perspective and experience, the context aims to ensure that everyone is using the same background and settings to interpret the research questions. To determine the criteria weights, an online survey was prepared and sent to cholera experts. The respondents were asked to "distribute 100 points across the five criteria according to the perceived level of importance, i.e., to allocate higher points to the criterion that they considered as the most important." The weights were determined by dividing the mean values allocated to each criterion by 20 (the value if each of the 100 points were distributed equally between the five criteria).

PHASE 2: IDENTIFYING THE RESEARCH PRIORITIES

More than 240 individuals were invited to score the 93 research questions using an online survey. The respondents were given the options of "Yes", "No", "Maybe" and "Don't know" when applying each criterion to each research question. Each response was assigned different point values of 1, 0 and 0.5 for "Yes", "No" and "Maybe", respectively, for the prioritization of the research questions. Questions for which the response was "Don't know" were excluded from the prioritization analysis. The following scores were calculated for each research question:

- **Weighted research priority score:** the following formula was used, where "W" is the weight for each criterion and "c" is the five criteria evaluating the research question. The following weights were applied: 0.79, 1.20, 1.12, 1.06 and 0.83 for answerability, impact, implementability, relevancy and sustainability, respectively.

$$\text{Weighted RPS} = \frac{1}{5} \times \sum_{c=1}^{5} W_c \times \frac{(N_{Yes} \times 1) + (N_{Maybe} \times 0.5)}{N_{Yes} + N_{No} + N_{Maybe}}$$

- **Average expert agreement scores:**[26] Average expert agreement is the average proportion of scorers that agreed on the five questions asked. The following formula was used, where "c" is the five criteria evaluating the research question.

$$\text{AEA} = \frac{1}{5} \times \sum_{c=1}^{5} \frac{N_{scorerswhoprovidedmostfrequentresponse}}{N_{scorerswhoprovidedanyresponse}}$$

Based on the weighted research priority scores, a rank was assigned to the research questions, where the highest research priority score received a rank of 1 and the lowest research priority score received a rank of 93.

Further stratified analyses considering certain perspectives were also conducted to evaluate potential biases in the final results. The stratified analyses included global[i] and regional/country perspectives (based on the respondent location).

[i] Global respondents were identified as being located in WHO's EURO or PAHO regions, except respondents in Haiti.

Annex C: Prioritization analysis of the 93 research questions

CE = Community engagement CM = Case management
OCV = Oral cholera vaccine WASH = Water, sanitation and hygiene

Rank	4D	Pillar	Research Question	Weighted Research Priority Score	Average Expert Agreement
1	Delivery	OCV	What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?	88.8%	80.7%
2	Delivery	OCV	What are potential delivery strategies to optimise oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?	87.4%	75.9%
3	Delivery	Cross-cutting (OCV, WASH)	Is there additional benefit to adding WASH packages, for example Household WASH kits, to an oral cholera vaccine campaign?	87.1%	77.2%
4	Delivery	OCV	What is the optimal number of doses of oral cholera vaccine to be used for follow up campaigns in communities previously vaccinated with a 2-dose schedule?	86.9%	76.4%
5	Delivery	OCV	Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?	86.8%	78.0%
6	Delivery	CM	What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?	86.8%	74.7%
7	Delivery	WASH	What levels of coverage for relevant water, sanitation and hygiene interventions is required in hotspots to control and ultimately eliminate the risk of cholera?	86.3%	74.9%
8	Delivery	OCV	What impact does the timing of oral cholera vaccine use have on the prevention and control of an outbreak?	86.2%	73.9%
9	Development	Epi / Sur / Lab	What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared to testing only in health facilities?	86.1%	74.6%
10	Delivery	OCV	How can the use of oral cholera vaccine in the controlled temperature chain (i.e., outside the cold chain) be leveraged to maximize the coverage or impact of vaccination in a field setting?	85.9%	75.2%
11	Delivery	Cross-cutting (all pillars)	What is the incremental benefit of implementing a comprehensive interventions package (including water, sanitation and hygiene, antibiotics, oral cholera vaccine, oral rehydration therapy) to reduce cholera mortality during an epidemic?	85.7%	74.3%
12	Delivery	OCV	What is the effectiveness and impact of different vaccination strategies for rapid response to cholera outbreaks (e.g., ring vaccination, case-area targeted interventions, etc.)?	85.3%	74.1%
13	Development	Cross-cutting (OCV, WASH)	What is the most cost-effective package of water, sanitation and hygiene and oral cholera vaccine in different situations based on transmission dynamics in cholera hotspots?	85.2%	73.7%
14	Development	WASH	What are the most essential (or what is the minimum set of) infection prevention and control (IPC) interventions in cholera treatment facilities and oral rehydration points to reduce risk of transmission within these facilities?	84.9%	74.2%
15	Delivery	OCV	Are there immunization strategies other than repeated mass campaigns that will be effective in preventing endemic or epidemic cholera?	84.9%	71.4%
16	Delivery	Cross-cutting	What is the role and added value of CORTs (community outreach response teams) in enhancing case investigation and outbreak detection?	84.6%	71.2%

Rank	4D	Pillar	Research Question	Weighted Research Priority Score	Average Expert Agreement
17	Development	OCV	Can the oral cholera vaccine be co-administered safely and without interference with other vaccines during mass campaigns or during routine immunization visits (measles containing vaccines, yellow fever, typhoid, meningitis, pneumococcal conjugate vaccine)?	84.3%	72.0%
18	Delivery	Cross-cutting (WASH, CE)	What are effective strategies to scale up the use of household water treatment in controlling cholera outbreaks?	84.1%	70.9%
19	Development	Epi / Sur / Lab	How can we improve and fine-tune hotspot definition and identification at a district and sub-district level?	84.1%	72.1%
20	Development	WASH	Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?	84.0%	74.1%
21	Development	Epi / Sur / Lab	What is (are) the optimal design(s) of surveillance systems (e.g., indicator-based, event-based, community-based, environmental, sentinel site surveillance) to monitor progress of the Cholera Roadmap?	83.8%	71.0%
22	Delivery	Cross-cutting (WASH, CE)	What are the factors, practices and behaviours that influence the uptake of different domestic hygiene or household interventions to support good hygiene and disinfection (or cleaning) practices for preventing and controlling cholera?	83.5%	69.8%
23	Development	CM	What effect does treatment with antibiotics have on cholera transmission?	83.3%	71.0%
24	Delivery	WASH	How can "design thinking" be used to improve the delivery/uptake of water, sanitation and hygiene interventions? Design thinking focuses on understanding the needs of the people who will use the intervention and working with them to improve it.	83.0%	67.4%
25	Description	OCV	What is the level and duration of herd protection from different vaccination schedules and strategies (e.g., one versus two doses, usefulness of annual single boosts to maintain herd protection, importance of vaccinating newcomers and former infants to maintain herd protection)?	83.0%	70.2%
26	Development	Epi / Sur / Lab	What are the optimal surveillance tools (e.g., laboratory methods, case definitions, etc.) to monitor progress of the Cholera Roadmap?	82.8%	69.6%
27	Delivery	Cross-cutting (WASH, CE)	What is the effectiveness of different approaches and delivery mechanisms to improve the uptake of hygiene promotion activities?	82.6%	68.0%
28	Delivery	Cross-cutting (CM, CE)	What are the optimal strategies to empower mothers and/or women to adopt preventive strategies and seek appropriate care for cholera?	82.6%	66.1%
29	Description	OCV	What are the factors influencing the duration of protection following use of oral cholera vaccine (includes target population and vaccination schedules)?	82.6%	67.5%
30	Development	OCV	What are the relative costs and cost-effectiveness of different oral cholera vaccine delivery strategies?	82.3%	68.8%
31	Development	Cross-cutting (all Pillars)	What is the effectiveness of different communication platforms for behaviour change programmes and risk communication in cholera prevention and control programmes?	82.3%	66.8%
32	Delivery	Cross-cutting (CM, CE)	How, when and where do people in the community seek care for cholera? What are the potential barriers (e.g., cultural and religious) to seeking timely cholera care?	82.1%	70.0%
33	Delivery	Cross-cutting (all pillars)	What is the required coverage and use level for each of the cholera interventions (including water, sanitation and hygiene, oral cholera vaccine, case management, and community engagement) needed to reduce transmission?	81.7%	67.7%
34	Delivery	Cross-cutting (CM, CE)	What are the solutions to overcoming the barriers (e.g., cultural and religious) to seeking timely cholera care?	81.7%	64.9%
35	Delivery	Cross-cutting (all pillars)	What are potential strategies to optimize cholera prevention and control interventions in hard-to-reach populations, including during humanitarian emergencies and areas of insecurity? (Examples can include: innovative contingency vaccination strategies, use of community-based teams to maintain front-line worker safety, engaging law enforcement agencies and military, etc.)?	81.4%	66.4%

Rank	4D	Pillar	Research Question	Weighted Research Priority Score	Average Expert Agreement
36	Description	Epi / Sur / Lab	How can combined epidemiological and genomic analysis of *V. cholerae* be used to better understand transmission dynamics and inform epidemiological models?	81.2%	67.6%
37	Delivery	Cross-cutting (OCV, CE)	What are prevailing knowledge, attitudes and practices in communities with respect to cholera vaccination?	80.9%	68.7%
38	Development	Cross-cutting (all pillars)	What is the impact and cost-effectiveness of the different interventions in case-area targeted interventions (CATI) and how can the impact be optimized?	80.9%	65.0%
39	Discovery	Epi / Sur / Lab	Research and development of novel and innovative diagnostic tests to accelerate the achievement of the Cholera Roadmap goals.	80.8%	65.9%
40	Development	Epi / Sur / Lab	What are the optimal methods/strategies for environmental surveillance for *V. cholerae*?	80.7%	66.1%
41	Development	OCV	What are the benefits and risks of vaccinating vulnerable populations in a cholera outbreak (some examples: pregnant women, the elderly, those with severe acute malnutrition)?	80.6%	68.7%
42	Development	CM	What is the optimal treatment schedule for antibiotic prophylaxis given to household contacts of cholera patients and does this have an effect on the magnitude, transmission and secondary attack rate of cholera outbreaks?	80.5%	69.7%
43	Development	OCV	What are the long-term impacts of oral cholera vaccine on disease severity and mortality from subsequent *V. cholerae* infections?	80.4%	64.7%
44	Delivery	WASH	What are the factors / determinants that lead to sustainable investments in water, sanitation and hygiene at country level?	80.3%	65.9%
45	Description	CM	What are the common cholera treatment complications in vulnerable populations (some examples: pregnant women, the elderly, those with severe acute malnutrition)?	80.2%	66.5%
46	Development	Cross-cutting (all pillars)	What is the relative and combined impact of different approaches (e.g. ,case-area targeted interventions (CATI), cluster-based approaches, hospital-based interventions, etc.) on cholera transmission and mortality at different stages of a cholera outbreak or in different contexts (e.g., during floods, in insecure areas or hard-to-reach populations)?	80.1%	63.4%
47	Development	CM	Would ReSoMal formulated with higher sodium, or standard oral rehydration solution containing high potassium, result in lower mortality or morbidity, compared with the standard WHO rehydration solution, in children with severe acute malnutrition?	80.1%	65.7%
48	Development	CM	What are valid and reliable hydration status assessment criteria in vulnerable patients with cholera (for example: pregnant women, the elderly, those with acute severe malnutrition)?	79.8%	64.9%
49	Discovery	OCV	Research and development of new or improved vaccines to contribute to accelerate the achievement of the Cholera Roadmap goals.	79.5%	64.7%
50	Development	CM	What is the role of nutritional support during a cholera outbreak, particularly for children?	79.5%	63.4%
51	Development	WASH	What are the most effective practices and technologies to collect, manage and dispose of cholera effluent, including identifying alternative technologies?	79.3%	66.6%
52	Delivery	Cross-cutting (All Pillars)	What are innovative models for promoting multisectoral collaboration for cholera prevention and control?	79.2%	62.1%
53	Description	Epi / Sur / Lab	What are the roles of short-term and long-term environmental reservoirs in the transmission of cholera?	78.6%	63.5%
54	Development	WASH	What is the impact and cost effectiveness on disease transmission of different components of the water, sanitation and hygiene package, considering different contexts?	78.4%	62.6%
55	Description	Epi / Sur / Lab	To what extent do asymptomatic infections contribute to transmission of cholera and to long-term latency of cholera in the community?	78.4%	61.5%

Rank	4D	Pillar	Research Question	Weighted Research Priority Score	Average Expert Agreement
56	Delivery	Epi / Sur / Lab	How can mobile alerts and social media platforms be used for detection and surveillance of cholera?	78.3%	59.9%
57	Description	CM	What are the underlying co-morbidities that increase the risk of poor cholera outcomes?	78.3%	62.5%
58	Development	Epi / Sur / Lab	Will community-based reporting by lay persons improve surveillance for cholera (where and how can it be used to optimize surveillance)?	77.9%	63.6%
59	Development	CM	Could zinc or other agents (e.g., boiled green bananas) play a role in reducing cholera severity and deaths in adults?	77.3%	60.7%
60	Delivery	Cross-cutting (all pillars)	What is the economic impact of cholera (including outbreaks) and the return on investments and budgetary impact of the various cholera interventions?	77.2%	62.4%
61	Delivery	Cross-cutting (CM, WASH)	Are there synergistic effects on cholera burden, transmission and mortality when antibiotic prophylaxis is combined with WASH?	77.0%	62.0%
62	Development	CM	What is the effectiveness of antibiotic treatment in vulnerable populations (some examples: pregnant women, the elderly, those with severe acute malnutrition) with cholera and with no or some dehydration?	76.5%	61.4%
63	Delivery	Cross-cutting (CM, CE)	How can we sensitize/motivate men to adopt preventive strategies and seek appropriate care for cholera?	76.1%	60.0%
64	Description	Epi / Sur / Lab	How does individual/community-level transmission dynamics of cholera compare with macro-scale (e.g., national/regional level) transmission dynamics in informing control strategies?	76.0%	56.8%
65	Description	Epi / Sur / Lab	What is the optimal number/proportion of cases that need to be laboratory confirmed during the different phases of a cholera outbreak?	75.9%	59.5%
66	Development	CM	What is the sensitivity and specificity of a composite clinical score for diagnosis of cholera in the community compared with cholera confirmed by rapid diagnostic test?	75.9%	60.0%
67	Development	CM	What are the benefits and risks of antibiotic prophylaxis in vulnerable populations in a cholera outbreak (e.g., pregnant women, the elderly, those with severe acute malnutrition)?	75.8%	61.1%
68	Description	Epi / Sur / Lab	What impact does implementing cholera control and prevention interventions in one setting or region have on long-range transmission routes and incidence of cholera in other areas (e.g., South Asia and Africa)?	75.7%	58.2%
69	Description	Epi / Sur / Lab	What are the extrinsic factors that influence the reproduction number of cholera (e.g., rainfall, crowding, etc.)?	75.7%	59.9%
70	Delivery	Cross-cutting (OCV, CE)	Do breast-feeding mothers who receive oral cholera vaccine transfer any level of protection, such as maternal antibodies, against cholera to their infants?	75.6%	58.7%
71	Development	CM	What effect does treatment with antibiotics versus no antibiotics have on mild cholera disease (e.g., diarrhoea with no signs of dehydration)?	75.5%	61.5%
72	Delivery	Cross-cutting (all pillars)	What is the effectiveness of different behaviour change theories and methods used in cholera prevention and control programmes?	75.1%	56.9%
73	Development	CM	What is the optimal treatment schedule for mass antibiotic prophylaxis in high-risk gatherings (e.g., refugee camps and prisons) and does this have an effect on the magnitude, transmission and secondary attack rate of cholera outbreaks?	75.0%	61.4%
74	Delivery	WASH	What is the role and effectiveness of applying public health policies and regulations (e.g., regarding food safety, open defecation and ban on surface water consumption) in controlling cholera outbreaks?	75.0%	59.1%
75	Delivery	OCV	Under what conditions would the creation of national stockpiles of oral cholera vaccine result in a cost-effective approach to cholera control?	75.0%	56.6%
76	Description	Epi / Sur / Lab	What should be the specific laboratory criteria and cut-off values (Minimum Inhibitory Concentration) for antibiotic susceptibility testing in *V. cholerae*?	74.5%	58.2%
77	Description	Epi / Sur / Lab	Can real-time modelling be used to conduct programme planning and optimize cholera outbreak response?	74.5%	57.0%

Rank	4D	Pillar	Research Question	Weighted Research Priority Score	Average Expert Agreement
78	Description	Epi / Sur / Lab	What are the phenotypic and genotypic characteristics of antibiotic resistance and what are the mechanisms of resistance in *V. cholerae*?	73.7%	56.6%
79	Description	CM	Does antibiotic resistance have an effect on severity of cholera?	73.7%	57.9%
80	Delivery	WASH	What is the relative impact of water, sanitation and hygiene investment on national and household budgets? Are the costs well-accepted?	73.4%	56.3%
81	Development	Cross-cutting (all pillars)	What are the indicators to measure the impact of behaviour change?	73.3%	54.8%
82	Development	CM	To what extent would large-scale use of antibiotic prophylaxis (either to prevent or respond to an outbreak) affect antimicrobial resistance (AMR) in *V. cholerae* and/or other pathogens (such as *E. coli* and *S. pneumoniae*)?	72.9%	56.1%
83	Discovery	Epi / Sur / Lab	Research to contribute to the collection of genomic data to create a global *V. cholerae* sequences database to map long-range transmission routes.	72.8%	55.7%
84	Description	Epi / Sur / Lab	What is the bacterial load of *V. cholerae* in different sample types/sources (including fresh stools) and how does this correlate with infectious dose, transmission and disease severity?	72.7%	58.4%
85	Development	CM	Does zinc prophylaxis prevent cholera when given to the contacts of a cholera index case?	71.9%	55.4%
86	Description	Epi / Sur / Lab	Can the epidemic potential of *V. cholerae* strains be predicted based on their genetic lineage and/or genomic data?	71.4%	53.9%
87	Delivery	WASH, CE	What are the optimal strategies, including behaviour change strategies, for delivering interventions related to safe burial practices and funeral hygiene?	71.0%	54.0%
88	Development	Epi / Sur / Lab	In what settings should serological surveillance be used to monitor cholera transmission? What would be the optimal study design and assays to use for these studies?	69.6%	54.2%
89	Development	CM	What proportion of patients have already received antibiotics before presenting to a cholera treatment centre and does this have an effect on outcomes?	69.3%	54.6%
90	Delivery	Cross-cutting (all pillars)	Is there stigma attached at individual level to cholera and the use of cholera interventions and does the stigma influence the disease reporting or uptake of interventions?	69.3%	53.8%
91	Development	WASH	What is the cost-effectiveness of food safety and food hygiene intervention for cholera prevention?	69.0%	51.2%
92	Description	CM	What is the risk of foetal loss during pregnancy in cholera patients?	65.7%	52.5%
93	Description	Epi / Sur / Lab	Does immunity have a role in the emergence of new strains of *V. cholerae* and what are the best immune markers and methods to explore this hypothesis?	65.7%	50.3%

Annex D: Provisional list of monitoring indicators for the Cholera Roadmap Research Agenda

A list of provisional indicators was developed in coordination with Wellcome Trust to monitor the progression of the Cholera Roadmap Research Agenda and the ability to fill identified evidence gaps.

Awareness
✗ The number of stakeholders who support the results of the Cholera Roadmap Research Agenda
✗ The number of stakeholders exposed to the Cholera Roadmap Research Agenda's messages
✗ The number of times the Cholera Roadmap Research Agenda is accessed through public websites.
Use and Uptake
✗ The number of funders aware of the Cholera Roadmap Research Agenda and the number of times funders utilize the Cholera Roadmap Research Agenda in their decision-making
✗ The number of times the Cholera Roadmap Research Agenda is used to plan and demonstrate relevancy of cholera research
✗ The number of prioritized research questions addressed in funded studies
✗ The number of cholera research funding grants allocated to prioritized research questions per the Cholera Roadmap Research Agenda
✗ The number of cholera-endemic countries with one or more funded research studies in line with the Research Agenda.
Outputs
✗ The number of research studies per prioritized research question that has been completed
✗ The number of times research outputs are communicated.

Annex E: Top twenty research priorities for respondents from cholera-endemic regions and countries

4D	Pillar	Research Question	Weighted Research Priority Score	Weighted Rank using. 138 responses	Average Expert Agreement
Delivery	OCV	Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?	95.8%	5	91.0%
Delivery	CM	What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?	94.3%	6	88.6%
Development	Epi / Sur / Lab	What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared to testing only in health facilities?	92.5%	9	86.9%
Delivery	OCV	What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?	92.4%	1	86.6%
Delivery	OCV	What are potential delivery strategies to optimize oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?	92.0%	2	83.8%
Delivery	WASH; CE	What are effective strategies to scale up the use of household water treatment in controlling cholera outbreaks?	91.8%	18	82.8%
Delivery	OCV; CE	What are prevailing knowledge, attitudes and practices in communities with respect to cholera vaccination?	91.7%	37	85.9%
Delivery	OCV; WASH	Is there additional benefit to adding WASH packages, for example household WASH kits, to an oral cholera vaccine campaign?	91.3%	3	83.3%
Development	Epi / Sur / Lab	What are the optimal methods / strategies for environmental surveillance for *V. cholerae*?	91.2%	40	84.6%
Delivery	WASH	What levels of coverage for relevant water, sanitation and hygiene interventions is required in cholera hotspots to control and ultimately eliminate the risk of cholera?	91.1%	7	81.7%
Delivery	CM; CE	How, when, and where do people in the community seek care for cholera? What are the potential barriers (e.g. cultural and religious) to seeking timely cholera care.	91.0%	11	83.3%
Delivery	All	What is the role and added value of CORTs (community outreach response teams) in enhancing case investigation and outbreak detection?	91.7%	12	82.4%
Delivery	All	What is the incremental benefit of implementing a comprehensive interventions package (including water, sanitation, and hygiene, antibiotics, oral cholera vaccine, oral rehydration therapy) to reduce cholera mortality during an epidemic?	90.3%	13	83.1%
Delivery	OCV	Are there immunisation strategies other than repeated mass campaigns that will be effective in preventing endemic or epidemic cholera?	90.3%	14	81.3%
Development	WASH	Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?	90.1%	15	81.7%
Delivery	OCV	What is the effectiveness and impact of different vaccination strategies for rapid response to cholera outbreaks (e.g., ring vaccination, case-area targeted interventions, etc)?	90.0%	16	81.5%
Development	OCV; WASH	What is the most cost-effective package of water, sanitation, and hygiene and oral cholera vaccine in different situations, based on transmission dynamics in cholera hotspots?	90.0%	17	82.2%

4D	Pillar	Research Question	Weighted Research Priority Score	Weighted Rank using. 138 responses	Average Expert Agreement
Delivery	CM; CE	What are the solutions to overcoming the barriers (e.g., cultural and religious) to seeking timely cholera care?	**89.8%**	**18**	**79.4%**
Delivery	All	What are innovative models for promoting multi-sectoral collaboration for cholera prevention and control?	**89.4%**	**19**	**79.4%**
Delivery	OCV	How can the use of oral cholera vaccine in the controlled temperature chain (i.e. outside the cold chain) be leveraged to maximize the coverage or impact of vaccination in a field setting?	**89.1%**	**20**	**80.9%**

Bibliography

1. Ali M, Nelson AR, Lopez AL, Sack DA. Updated global burden of cholera in endemic countries. PLoS Negl Trop Dis 2015; 9(6): e0003832-e.
2. World Health Organization. Cholera: 2018. Weekly epidemiological record 2019; 48(94): 561-80.
3. Global Task Force on Cholera Control. Ending cholera – A global roadmap to 2030, 2017.
4. World Health Organization. Cholera vaccines: WHO position paper – August 2017. Weekly epidemiological record 2017; 34(92): 477-500.
5. Interim Technical Note – The Use of Cholera Rapid Diagnostic Tests. Geneva: The Global Task Force on Cholera Control, 2016.
6. World Health Organization. Cholera, 2019. Weekly epidemiological record 2020; 37(95): 441-8.
7. Rudan I, Yoshida S, Chan KY, et al. Setting health research priorities using the CHNRI method: I. Involving funders. Journal of Global Health 2016; 6(1).
8. Yoshida S, Cousens S, Wazny K, Chan KY. Setting health research priorities using the CHNRI method: II. Involving researchers. Journal of Global Health 2016; 6(1).
9. Yoshida S, Wazny K, Cousens S, Chan KY. Setting health research priorities using the CHNRI method: III. Involving stakeholders. Journal of Global Health 2016; 6(1).
10. Rudan I. Setting health research priorities using the CHNRI method: IV. Key conceptual advances. Journal of Global Health 2016; 6(1).
11. Rudan I, Yoshida S, Wazny K, Chan KY, Cousens S. Setting health research priorities using the CHNRI method: V. Quantitative properties of human collective knowledge. Journal of Global Health 2016; 6(1).
12. Yoshida S, Rudan I, Cousens S. Setting health research priorities using the CHNRI method: VI. Quantitative properties of human collective opinion. Journal of Global Health 2016; 6(1): 1-9.
13. Rudan I, Yoshida S, Chan KY, et al. Setting health research priorities using the CHNRI method: VII. A review of the first 50 applications of the CHNRI method. J Glob Health 2017; 7(1): 011004.
14. Rudan I, Gibson JL, Ameratunga S, et al. Setting priorities in global child health research investments: guidelines for implementation of CHNRI method. Croat Med J 2008; 49(6): 720-33.
15. Rudan I, Chopra M, Kapiriri L, et al. Setting priorities in global child health research investments: universal challenges and conceptual framework. Croat Med J 2008; 49(3): 307-17.
16. A systematic approach for undertaking a research priority setting exercise: Guidane for WHO Staff. Geneva: World Health Organization, 2020.
17. GTFCC Research Agenda - Scoping Meeting. Geneva: Global Task Force on Cholera Control, 2018.
18. Finger F, Bertuzzo E, Luquero FJ, et al. The potential impact of case-area targeted interventions in response to cholera outbreaks: A modeling study. PLoS Medicine 2018; 15(2): 1-27.
19. Global Task Force on Cholera Control Surveillance Working Group. Interim Guidance Document on Cholera Surveillance Global Task Force on Cholera Control (GTFCC) Surveillance Working Group. Geneva, 2017.
20. Rapid response teams: A UNICEF experience. New York: UNICEF, 2019.
21. The American Heritage® Medical Dictionary: Houghton Mifflin Company; 2007.
22. Cambridge Dictionary. Cambridge; 2020.
23. International Classification of Health Interventions (ICHI). Geneva: World Health Organization, 2020.
24. Cholera Outbreak Response: Field Manual. Geneva: Global Task Force on Cholera Control, 2019.
25. Management of severe acute malnutrition in infants and children, WHO recommendations. Geneva: World Health Organization.
26. Arora NK, Mohapatra A, Gopalan HS, et al. Setting research priorities for maternal, newborn, child health and nutrition in india by engaging experts from 256 indigenous institutions contributing over 4000 research ideas: A CHNRI exercise by ICMR and INCLEN. Journal of Global Health 2017; 7(1).

GLOBAL TASK FORCE ON
CHOLERA CONTROL